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Equilibrium binding interactions between lotrafilcon a soft contact lenses and the two prostaglandin anti-glaucoma drugs bimatoprost and tafluprost

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Objectives: To determine equilibrium binding constant (EB) values for bimatoprost and tafluprost drug product formulations in contact with Lotrafilcon A soft contact lenses and to characterize the importance of drug molecule hydrophobicity in controlling binding interactions

Methods: Bimatoprost Ophthalmic Solution and Tafluprost Ophthalmic Solution (Saflutan®) drug product solutions were incubated with Lotrafilcon A lens material for timed intervals at 25 and 37 °C. Aliquots were withdrawn, filtered and tested by RP-UPLC with respect to [bimatoprost] or [tafluprost] remaining in solution. A series of homologous dialkyl phthalate esters and a series of homologous p-hydroxybenzoic acid alkyl esters were also tested as reference compounds.

Results: Bimatoprost and tafluprost were both rapidly (within 15 min) absorbed from solution by Lotrafilcon A lenses, reaching equilibrium within 60 min. At any lens:solution(w/v) ratio, the extent of drug binding to lens material was greater for tafluprost than for bimatoprost. The log(EB) values correlated with solute octanol:water partition coefficient (logP) values, indicating that hydrophobic interactions are important in controlling solute partitioning into the lens material.

Conclusions: This study established quantitative relationships for tafluprost and bimatoprost binding to Lotrafilcon A lenses. The fraction of either bimatoprost or tafluprost that binds to Lotrafilcon A increases with increasing lens:solution (w/v) ratio. For a 60-μL dose volume applied to a single contact lens, 16% of initially-present bimatoprost remains in solution, whereas only 6% of initially-present tafluprost remains in solution. These calculations clearly demonstrate that both drugs partition very extensively into Lotrafilcon A contact lens material. Although the clinical implications of such binding can only be surmised, it would seem prudent to caution contact lens wearers to remove the lenses before administering either prostaglandin drug.

Biography

Richard Kenley, Ph.D. (Advantar founder and CEO), has over 30 years experience in the pharmaceutical, biotechnology, and bio-pharma contract service industries. He is an inventor on 4 patents, author of over 60 peer-reviewed scientific publications. Dr. Kenley has made major contributions to the development and eventual approval of important pharmaceuticals including: butaconazole, nafarelin (Synarel®), bone morphogenetic protein 2 (InFuse®), rhIL-11 (Neumega®), pramlintide (Symlin®), and exenatide (Byetta®). His industry assignments include senior management positions at SRI International, Syntex, Baxter, Genetics Institute (Pfizer), Amylin (Astra-Zeneca), and Cabrillo Laboratories (Catalent).

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